

New Approaches to Natural Products Drug Discovery

*Profiting from Biodiversity in
Combination with New Targets*

An International Conference

November 12-14, 1997

The Renaissance Harborplace Hotel • Baltimore, MD

Plus

Chemical Analysis of BioPharmaceuticals & Regulatory Issues

A Pre-Conference Symposium • November 12, 1997

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*Learn how to reliably and rapidly
identify more useful lead
compounds from natural sources*

New Approaches to Natural Products Drug Discovery

The Renaissance Harborplace Hotel, Baltimore, MD November 13-14, 1997

PROGRAM AGENDA

Thursday, November 13, 1997

8:00 Registration, Poster and Exhibit Set-Up

8:30 Chairperson's Opening Remarks

Alice M. Clark, Ph.D., Director, National Center for the Development of Natural Products and F.A.P. Distinguished Professor of Pharmacognosy, University of Mississippi

Extract Libraries, Screenings & Assays

8:40 Decisions, Decisions! Reconciling the Search for Mechanistically and Structurally Novel Natural Products with High Throughput Screening

Alice M. Clark, Ph.D.

9:10 Extract Banks and High Throughput Screening

Salvatore Forenza, Ph.D., Director, Automation Technologies & Natural Products Research, Bristol-Myers Squibb

9:40 Effective Search of New Therapeutics from Microbial Fermentation ✓

May D. Lee, Ph.D., Associate Director, Molecular Diversity, Microcide Pharmaceuticals, Inc.

10:10 Poster and Exhibit Viewing and Refreshment Break

10:40 Integrated Screening Technologies for Combinatorial Biology-Based Drug Discovery Programs

Paul Brian, Ph.D., Research Scientist, ChromaXome Corporation, A Trega Biosciences Company

11:10 Affinity-Based Homogeneous Assays: A New Screening Paradigm for High-Throughput Drug Discovery from Complex Matrices

Reimar C. Bruening, Ph.D., RPh, Vice President, Natural Products Chemistry, Millennium Pharmaceutical

11:40 Networking Luncheon

1:10 The Genetic Analysis of Marine Actinomycete Secondary Metabolic Genes and Their Associated Products

Bradley S. Moore, Ph.D., Research Assistant Professor, University of Washington

1:40 Rational Intervention in Aging

William Regelson, M.D., Professor of Medicine, Director of the Program for Successful Aging, Medical College of Virginia, Virginia Commonwealth University

2:10 Chiroptical Spectroscopy: A Powerful Tool for Structural Studies of Bioactive Compounds

Nina Berova, Ph.D., Dept. of Chemistry, Columbia University

2:40 Poster and Exhibit Viewing and Refreshment Break

3:10 The Discovery of Novel Therapeutics via Plant Cell Culture

James McAlpine, Ph.D., Director of Natural Products Chemistry, Phytera, Inc.

3:40 Strategies for Accelerated Natural Products Discovery Programs

Jeff W. Paslay, Ph.D., Senior Director Drug Discovery Services, MDS Panlabs

Chemical Purification

4:10 Production of Hybrid Glycopeptide Antibiotics Using Cloned

Glycosyltransferase Genes

Richard H. Baltz, Ph.D., Research Advisor, Lilly Research Laboratories

4:40 The Venomous Cone Snail: Evolutionary Success through Drug Development

Baldomero Oliveria, Ph.D., Distinguished Professor of Biology, University of Utah

5:10 Chairperson's Remarks

5:15 Close of Day One

Friday, November 14, 1997

Active Natural Products

7:30 Poster and Exhibit Viewing and Networking Continental Breakfast

8:00 Chairperson's Summary of Day One and Opening Remarks

Ross E. Longley, Ph.D., Group Leader, Immunology, Oncology and Screening, Division of Biomedical Marine Research, Harbor Branch Oceanographic Institute

8:05 Transgenic Approaches to Identifying Compounds from Unculturable Fungi

Eneida H. Pardo, Ph.D., Post-doctoral fellow, Millennium Pharmaceuticals, Inc.

8:35 Cladistics and Congruence: Innovative Approaches to Biodiversity Prospecting

Dennis W. Stevenson, Ph.D., Director, Harding Laboratories, New York Botanical Garden
Douglas C. Daly, Ph.D., Associate Curator, New York Botanical Garden

9:05 Poster and Exhibit Viewing and Refreshment Break

9:35 Pharmaceuticals and Biologically-Active Compounds Produced by Fungi

Cedric Pearce, Ph.D., Director of Fermentation, MYCOsearch

10:05 Bioactive Compounds from Amphibians

John W. Daly, Ph.D., Chief, Laboratory of Bioorganic Chemistry, NIDDK, NIH

New Approaches for Discovery

10:35 Chairperson's Remarks

Jon Clardy, Ph.D., Professor, Dept. of Chemistry, Cornell University

Keynote Address

10:40 Genetic Engineering and Chemo-biosynthesis in the Polyketide Synthase Pathway

Daniel V. Santi, Ph.D., M.D., Chairman, Kosan Biosciences, Inc.

11:25 Lunch on Own

12:45 Soil Microbial Diversity and Antibiotic Discovery

Jo Handelsman, Ph.D., Department of Plant Pathology, University of Wisconsin-Madison

1:15 Combinatorial Genomics and Natural Product Drug Discovery

Peter Carlson, Ph.D., Vice President, Oceanix Biosciences Corporation

1:45 Exploring the Uncultured Microbial World for Novel Natural Products.

Joseph McDermott, Ph.D., Director of Technology, TerraGen Diversity Inc.

2:15 Poster and Exhibit Viewing and Refreshment Break

2:45 The Chemical and Genetic Diversity of Marine Microalgae: An Exciting Resource

Jeffrey L.C. Wright, C.M., Ph.D., Senior Research Officer, National Research Council (NRC)

3:15 Discovery of Antitumor and Immunomodulating Compounds from Marine Organisms

Ross E. Longley, Ph.D

3:45 Natural Products Drug Discovery and Development: The NCI Role

Gordon Cragg, Ph.D., Chief, Natural Products Branch, National Cancer Institute

4:15 Natural Products and their Macromolecular Targets

Jon Clardy, Ph.D

4:45 Chairperson's Closing Remarks

5:00 Close of Conference

POSTER ABSTRACTS

Natural Products

METHODOLOGY FOR THE DETECTION OF BIO-ACTIVE ALLELOCHEMICAL COMPOUNDS IN MEXICAN PLANTS ¹

Anaya, A.L.^{1,2}, R. Cruz-Ortega¹, B.E. Hernández-Bautista¹, A. Torres-Barragán¹, G. Ríos¹, C. Flores-Carmona¹, M. Calera-Medina¹, A. Arévalo-Barajas¹, H.R. Pelayo-Benavides¹, S. del Amo², and A. Gómez-Pompa³.

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2. Gestión de Ecosistemas, A.C., México
3. University of California, Riverside. U.S.A.

Allelopathy is a complex science in which different disciplines interact. Different kind of secondary compounds are involved in the allelopathic phenomenon. The growing interest in allelopathy is partially due to the discovery and application of novel compounds that can control weeds, pests, and diseases, without damaging the environment. One of the objectives in allelopathy studies is to detect -using different type of bioassays- the allelochemicals that affect the growth of other organisms, isolating and identifying them. Chemical structure of allelochemicals can be modified, and such changes can either increase or decrease their biological activity. In the present study we describe a methodological model that is being used to study allelochemicals produced by different plant species from Mexico. This model is based on different bioassays to evaluate the allelopathic potential of species and to follow the activity during extraction, purification, and identification of bioactive compounds.

The procedure followed includes:

The aqueous leachate, organic extracts and pure compounds of plants are tested on:

1. Seed germination and radicle growth of test species (*Amaranthus hypochondriacus* and *Echinochloa crusgalli*). These two species represent the two major groups of Angiosperms: monocotyledonous and dicotyledonous. Bioautography Tests are applied in these bioassays. Extracts of plants are separated by TLC. Plates are covered with a thin layer of agar and *Amaranthus* seeds are sowed on them. Germination and radicle growth are evaluated.
2. Bioassays using phytopathogenic fungi, brine shrimp lethality test, insects, and nematodes are also used to evaluate the bio-activity of allelochemicals from the plants.
3. Greenhouse experiments are carried out to evaluate the effect of allelochemicals on crops and weed growth, mycorrhizae and *Rhizobium* establishment.
4. Some mode of action of the allelochemicals are also studied (photosynthesis, respiration, enzyme activity, cell division, protein synthesis, and gene expression).

¹ This study is partially sponsored by USDA (FG-Mx-107/MX-AES-6).

A Strategic DR Report on How to Optimize this Rapidly Growing Market...

Plant- and Marine-Derived Pharmaceuticals: Discovery and Development

Plant- and Marine-Derived Pharmaceuticals is a sourcebook of data and analysis about the cost, timelines, and techniques involved in the discovery and development of plant- and marine-sourced drugs. This report discusses:

- Companies at the forefront.
- Products and their prospects.
- Appropriate technology partners.
- The libraries, databases, and pharmaceuticals that provide the compound leads.
- Organizations involved in collection of plant samples.
- Major commercialized drugs derived from plants.
- Plant-derived compounds in research and development investigation.
- Companies specializing in technology and synthesis of component drugs derived from plants.
- Strategies for screening plants.

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A Strategic DR Report on how to Dominate this Rapidly Growing Market.

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- Plant-derived compounds in relatively advanced stages of investigation.
- Companies specializing in technology and single-component drugs derived from plants.
- Strategies for screening plants.

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